II. REMARKS

Formal Matters

Claims 10-24 and 28-30 are pending after entry of the amendments set forth herein.

Claims 10-13 were examined and were rejected. Claims 14-24 were withdrawn from consideration.

Claim 10 is amended. The amendments to claim 10 were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claim 10 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: page 11, line 24 to page 12, line 6; and page 14, lines 3-4; page 5, line 22 to page 6, line 15; and the Examples. Accordingly, no new matter is added by these amendments.

Claims 28-30 are added. Support for new claims 28-30 is found in the claims as originally filed, and throughout the specification, including the following exemplary locations: claim 29: page 11, lines 27-29; claims 29 and 30: page 12, lines 6-7. Accordingly, no new matter is added by these new claims.

Applicant respectfully requests reconsideration of the application in view of the remarks made herein.

Examiner Interview

The undersigned Applicant's representative wishes to thank Examiner Winkler for the courtesy of a telephonic interview, which took place on October 7, 2003, and which was attended by Examiner Winkler, inventor Dr. S. Finkbeiner, and Applicant's representative Paula A. Borden. During the interview, the enablement rejection of claims 10-13 under 35 U.S.C.§112, first paragraph, was discussed. The remarks made below reflect the discussion of the enablement rejection during the telephonic interview.

Objection to the specification

The Office Action stated that Applicant is required to update the status of all parent priority applications in the first line of the specification. Applicant respectfully requests entry of the above-noted amendment to the specification, which amendment updates the status of the prior application.

Claim objections

The Office Action objected to claim 10 as depending from a canceled claim.

Claim 10 is amended so that it no longer recites an antibody "according to Claim 1," thereby adequately addressing this objection.

Rejection under 35 U.S.C.§112, second paragraph

Claims 10-13 were rejected under 35 U.S.C.§112, second paragraph, as allegedly indefinite.

The Office Action stated that in claim 10, it is not clear what is intended by "a target."

Without conceding as to the correctness of this rejection, claim 10 is amended to recite "wherein the ability of an agent to modulate the binding interaction between said protein and said antibody indicates that the ability of said agent to modulate the binding interaction between said protein and a cellular target of said protein."

The Office Action stated that in claim 10, it is not clear what is intended by "a first compound that is said protein or binding fragment or mimetic thereof."

Without conceding as to the correctness of this rejection, claim 10 is amended to recite "contacting said protein or a binding fragment or mimetic thereof."

Applicant submits that the rejection of claims 10-13 under 35 U.S.C. §112, second paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§112, first paragraph

Claims 10-13 were rejected under 35 U.S.C.§112, first paragraph, as allegedly not enabled. Applicant respectfully traverses the rejection.

The Office Action stated that the methods cannot distinguish whether the agent binds to the antibody or the polyglutamine-containing protein. As discussed during the Examiner Interview, it is not required that the methods distinguish whether an agent binds to the antibody or to the polyglutamine-containing protein. The claim only requires that the agent modulate binding interaction between an antibody and a polyglutamine expansion of a polyglutamine expansion-containing protein, which

indicates that the agent modulates a binding interaction between a polyglutamine expansion-containing protein and a cellular target of the protein.

The Office Action stated that there is no correlation in the prior art or in the instant specification that would indicate that a compound that interferes with the antibody binding to the polyglutamine expansion of huntingtin would interfere with the antibody binding to the polyglutamine expansion protein to the normal cellular target. However, the specification states that agents identified by the claimed method inhibit the binding interaction between the polyglutamine expansion-containing protein and a cellular target of the protein. Specification, page 11, lines 24-29. Those skilled in the art would find it reasonable to expect that an agent that modulates binding interaction between an antibody and a polyglutamine expansion of a polyglutamine expansion-containing protein would also modulate a binding interaction between a polyglutamine expansion-containing protein and a cellular target of the protein. Antibodies are proteins, and the cellular target of the polyglutamine expansion-containing protein is expected to be a protein. The antibody binding pocket is expected to be a mimic for a cellular target of a polyglutamine expansion-containing protein. In view of such, those skilled in the art would expect that the binding interaction between an antibody to a polyglutamine expansion of a polyglutamine expansion-containing protein would serve as a surrogate for the binding interaction between a polyglutamine expansion-containing protein and a cellular target of the protein.

Illustrative of the principle that an antibody that is specific for a protein can serve as a surrogate, or a model, for the binding interaction between that protein and a second protein are the following references: Kaji et al. ((2001) *J. Biochem.* 129:577-583; "Kaji"; a copy of which is provided herewith as Exhibit 1); and South et al. ((1995) *Thromb. Haemost.* 73:144-150; "South"; a copy of which is provided herewith as Exhibit 2).

Kaji discusses screening a phage display library with monoclonal antibodies that inhibit the chemotactic activity of monocyte chemoattractant protein-1 (MCP-1). Phage clones that were bound by the antibodies were isolated and characterized. Two peptides were identified that bound to THP-1 cells (which are responsive to MCP-1); the binding was competitively inhibited by MCP-1. Kaji concluded that the peptides mimic the MCP-1 binding domain that is recognized by the MCP-1 receptor. Thus, Kaji successfully used antibody binding to domain on the MCP-1 protein as a surrogate, or a model, for the binding of the MCP-1 protein to its cellular target, i.e., the MCP-1 receptor.

South discusses screening a phage display library for inhibitors of the von Willebrand factor (vWF)-platelet Glycoprotein Ib (GPIb) interaction. The phage display library was screened with a monoclonal antibody that recognizes the GPIb binding domain of vWF. Phage clones were identified that reacted with the monoclonal antibody. A number of the peptides thus identified inhibited binding of vWF to GPIb. Thus, South successfully used antibody binding to a domain of vWF as a surrogate, or a model, for vWF-GPIb binding; and, using the monoclonal antibodies, successfully identified peptides that inhibited vWF-GPIb binding.

The Office Action stated that Heiser et al. ((2000) *Proc. Natl. Acad. Sci. USA* 97:6739-6744; "Heiser") teaches that the monoclonal antibody (MAb) 1C2 specifically recognizes polyglutamine expansions in soluble huntingtin, and that the MAb does not recognize insoluble high molecular weight polyglutamine expansions. As discussed during the Examiner Interview, the claims recite use of a monoclonal antibody that recognizes a protein having a polyglutamine expansion and that binds to a polyglutamine expansion-containing protein in a manner that differs from the 1C2 antibody. During the Examiner Interview, amendment of claim 10 to recite that the antibody binds with greater affinity than does the 1C2 MAb was discussed.

The specification describes in ample detail how to determine whether a given agent modulates binding between a polyglutamine expansion-containing protein and an antibody. Those skilled in the art could readily determine whether such an agent also modulates binding between the polyglutamine expansion-containing protein and its cellular target. Accordingly, those skilled in the art could use the invention as claimed.

Applicant submits that the rejection of claims 10-13 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL161DIV.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: Oct. 20, 2003

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